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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,613	01/03/2002	Y Tom Tang	PF-0711 USN	8308

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EXAMINER	
SAIDHA, TEKCHAND	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 02/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,613	TANG ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-7,9 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-7, 9 & 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Applicants' Amendment filed 12.09.2003 is acknowledged.

2. **Claims 3-7, 9 and 11** [SEQ ID NO : 3 encoding SEQ ID NO : 1] are under consideration in this Office Action.

3. Claims 8, 12, 14, 15, 18, 20-21, 23-24, 26-27, 29-60 have been canceled by the listing of the claims that replaces all prior versions of the claims, as per the above amendment.

4. Claims 1-2, 10, 13, 16-17, 19, 22, 25 & 28 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, as per the above amendment.

5. Applicant's arguments filed as per the amendment cited above have been fully considered but they are not deemed to be persuasive or are moot in view of the new ground(s) of rejection. The reasons are discussed following the rejection(s).

6. Any objection or rejection of record which is not expressly repeated in this Office Action has been overcome by Applicant=s response and withdrawn.

7. ***Objection***

Claims 4-5, 9 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims depend from claims which have been withdrawn following lack of unity.

8. The Examiner notes that if product claims in Group III are found directed to an allowable product, then process claims in Group III, which are directed to processes of making or **using the patentable product** [i.e. the DNA sequence of SEQ ID NO : 3, covering the **same scope** as of the allowable product)], respectively, previously withdrawn from consideration as a result of a restriction requirement, would now be rejoined pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86; see also M.P.E.P. □ 821.04, *In re* Ochiai, and *In re* Brouwer). Since process claims would be rejoined and fully examined for patentability under 37 C.F.R. □ 1.104, Applicants are instructed to amend said claims as deemed necessary according to rejections made against the elected claims.

9a. ***New Matter***

The amendment filed 12.09.2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: For example, Claim 3, lines 6 & 8 recite **'phosphate inhibitory activity'** .

Applicant is required to cancel the new matter in the reply to this Office Action.

9b. ***Written Description***

Claims 4, 9 & 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are

directed to a genus of DNA (or polynucleotide) molecules with either SEQ ID NO: 3 having the limitation of encoding a protein which is 90% identical to the sequence of SEQ ID NO: 1, with no defined function, or a method of making such a protein or any DNA sequence which 90% identical to SEQ ID NO : 3.

The specification does not contain any disclosure or description of the structure and function of all DNA sequences that are 90% identical to SEQ ID NO : 3, or DNA that encode polypeptide(s) that 90% identical to SEQ ID NO : 1 or use such a DNA in the method of making polypeptide(s) that 90% identical to SEQ ID NO : 1 (claims 4, 9 & 11). Further, the specification as filed does not describe specific assays to measure the various polypeptide sequences having the 'phosphatase inhibitory activity' or which is so evident, as none is described. Assay measuring ß-galactosidase activity of a DETX molecule is described. No phosphatase inhibitory activity was even shown to associated with the DETX molecule(s). The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only 2 species as human detoxification proteins (DETX1 and DETX2) of the claimed genus with defined function known which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicants' Arguments:

Applicants argue that the requirement to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, are well established case law..... 'the Applicants must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-cath, Inc. v. Mahurkar,* 19 USPQ2d 1111, 1117 (Fed. Cir.1991)

Applicants' further point to – Patent and Trademark Office's own "Guidelines for Examination of Patent Application under the 35 USC Sec. 112, paragraph 1", published January 5, 2001, which provide that :

An Applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in passion of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a claimed invention at the time of filing, even if every nuance of the claim s is not explicit described in the specification, then the adequate description requirement is met.

Based upon the above cited case law and the USPTO Guidelines for Written Description rejection, Applicants state - "Thus the written description standard is fulfilled by both what is specifically disclosed and is conventional or well known in the prior art.

In response it is pointed out that Applicants' arguments are well founded as far as what is disclosed – which are the sequences of SEQ ID N0: 1 and SEQ ID NO: 3. Unfortunately, there are no variants described on pages 2 (lines 26-34) and 22 (lines 10-18). Incyte clones are exemplified in Tables 2 & 4. Neither clear cut guidance, nor even a single example is provided as to what regions/motifs/nucleotides of the sequence(s) are modified without impairing the functionality of the DETX protein in order to create a sequence having 90% identity with respect to SEQ ID NO : 1 or 3. Therefore based upon the data provided, i.e. the sequences of SEQ ID Nos. 1 & 3, one skilled in the would recognize, or modify sequences by 10% and still obtain a functional DNA capable of encoding a detoxification protein, for which no clear assay is described and for which no clear functional basis is evident, written description remains unsupported both in the context of *Vas-cath, Inc. v. Mahurkar,* 19 USPQ2d 1111, 1117 (Fed. Cir.1991) as well as US Patent and Trademark Office's "Guidelines for Examination of Patent Application under the 35 USC Sec. 112, paragraph 1", published January 5, 2001.

Applicants are further misplaced in their arguments that since the claims are directed to polynucleotide it is the functionality of the claimed polynucleotide, not the encoded polypeptide that is relevant.

In response, it is pointed out that the claims are directed to isolated modified polynucleotide(s), wherein such modifications are neither taught nor described, and wherein such modified or variant polynucleotides may or may not necessarily encode a functional protein. Therefore, the functionality of the claimed polynucleotide is as vital as

that of the polypeptide it encodes. Therefore, the written description requirements, as per the Patent and Trademark Office's "Guidelines for Examination of Patent Application under the 35 USC Sec. 112, paragraph 1", published January 5, 2001, are not met.

9c. Claims 3-7, 9 & 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide sequence of SEQ ID NO: 3, encoding a human detoxification protein [or DETX1] polypeptide sequence of SEQ ID NO : 1, does not reasonably provide enablement for any polynucleotide having 90% identity to SEQ ID NO: 3 or a polynucleotide encoding a polypeptide having at least 90% sequence identity to the amino acid sequence of SEQ ID NO : 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the claims does not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide [SEQ ID NO : 3] and encoded amino acid sequence of SEQ ID NO : 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of any DNA with 90% identity to the DETX1 protein of SEQ ID NOS: 1, because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting DETX1 protein activity; (B) the general tolerance of DETX1 protein to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any DETX1 protein residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

This is further supported by Applicants' recent BLAST analysis showing that SEQ ID NO: 1 is 99% identical to the calcineurin inhibitor ZAKI-4 (g21307625) [Cao et al. Biochem. J. 367 : 459-466 (2002)], where an actual showing of the function is evident by experimentation. As can be clearly seen from Applicants' recent BLAST analysis a 1% difference or change in the sequence identity i.e. between ZAKI-4 and DETX1 (EQ

ID NO : 1), completely changes the functionality of the polypeptide from being a calcineurin inhibitor to a human detoxification protein. Thus there is high unpredictability associated with respect to modification(s) of the sequence of SEQ ID NO : 1, resulting from modification of the polynucleotide(s) encoding proteins of varying or no function(s).

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of exact nature DETX1 protein encoding DNA (or polynucleotide) having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue in using the modified enzyme in the method claimed. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

10. Claims 3, 6-7 & 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 (line 4) & claim 11 (line 5), recite the phrase "naturally occurring". The claims are indefinite because it contradicts the limitation(s) in the opening phrase of the claims 'isolated'. Deleting the phrase "naturally occurring" is suggested to overcome this rejection.

11. ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 3-7, 9 & 11 are rejected under the judicially created doctrine of double patenting over claims 1-13 of U. S. Patent No. 6,524,819 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application [common assignee, different inventors] are claiming common subject matter, as follows: Applicants' Polynucleotide (SEQ ID NO : 3) encoding the polypeptide of SEQ ID NO : 1

is disclosed in the cited patent and is 100% identical, is comprised by the polynucleotide sequence of SEQ ID NO : 1 (or encoding the polypeptide sequence of SEQ ID NO : 2) disclosed in cited USP '819. The reference anticipates the claims.

As per Applicants' request the requirement is held in abeyance until there is indication of allowable subject matter.

12. Claims 3-7, 9 and 11 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

Applicants disclose a nucleic acid sequences (SEQ ID NO: 3) encoding the amino acid sequence of SEQ ID NO: 1. Based on reasonable sequence homology, the polypeptide of SEQ ID NO: 1 is sought to be a human detoxification protein (DETX) which is a generic asserted utility. human detoxification protein belong to no known family of enzymes or proteins involve in any specific biological process(es). It is nearly impossible from sequence homology alone to attribute a specific and substantial function for the protein. Even accepting the plausible utility of being a human detoxification protein, one of ordinary skill in the art would not know which compound(s) are detoxified by the polypeptide. The specification does not disclose a specific function of the polypeptides of SEQ ID NO: 1, its relationship to any disease, or any specific real world use. The specification describes generic functions for the protein, nucleic acid, and antibodies. The utility of the variant nucleic acid is said to be associated with encoding defective polypeptides, wherein the variants are associated with disease

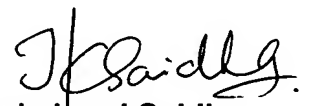
state, such as the diseases listed on page 45-46. It appears that the main utility of the polypeptide and nucleic acid is to carry out further research to identify the biological function and possible diseases associated with said function. Substantial utility defines a real world use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a real world context of use are not substantial utility. Thus, the claimed invention has no specific or substantial asserted utility.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (571) 272-0940. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group in the Technology Center is 703 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 571 272-1600.



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